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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/688,759

10/17/2003

Santosh R. D'Mello

UTDA:1141

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09/30/2010

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EXAMINER

CRUZ, KATHRIEN ANN

ART UNIT

PAPER NUMBER

1628

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b><i>Advisory Action Before the Filing of an Appeal Brief</i></b>	<b>Application No.</b> 10/688,759	<b>Applicant(s)</b> D'MELLO ET AL.	
	<b>Examiner</b> KATHRIEN CRUZ	<b>Art Unit</b> 1628	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 16 September 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
 b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
 (b) ☐ They raise the issue of new matter (see NOTE below);  
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
 (d) ☒ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
 5. ☒ Applicant's reply has overcome the following rejection(s): 35 U.S.C.112, first paragraph.  
 6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
 The status of the claim(s) is (or will be) as follows:  
 Claim(s) allowed: \_\_\_\_\_.  
 Claim(s) objected to: \_\_\_\_\_.  
 Claim(s) rejected: 12, 14, 15, 17-34.  
 Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: \_\_\_\_\_.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_
13. ☒ Other: Applicants argue that a prima facie case of obviousness has not been established. This argument has been fully considered but has not been found persuasive. Sweatt teaches that the amount of activated MAPK in a neuron can be reduced by approaches that cause dephosphorylation of upstream kinases in the MAPK cascade. Thus, compounds that activate phosphatases specific for any members of the MAPK cascade upstream of MAPK will reduce the activity of the upstream kinase, ultimately leading to reduced downstream activity of MAPK. Compounds that effect dephosphorylation of other upstream kinases including Ras, Raf1 (also known as c-raf), B-Raf and Rap1 may be used (paragraph 0027). Hall-Jackson teaches that N-[5-(3- Dimethylaminobenzamide)-2-methylphenyl]-4-hydroxybenzamide (herein after, "ZM 336372") is a potent and specific inhibitor of c-Raf that shows a tenfold selectivity over B-Raf (page 565, first paragraph under Discussion). It would have been obvious to one of ordinary skills in the art at the time of the invention was made to employ the specific c-Raf, ZM 336372 to treat epilepsy (seizure disorder) or individuals susceptible to neurodegenerative disease. One would have been motivated to employ ZM 336372 because ZM 336372 is a potent and effective inhibitor of c-raf and B-raf as taught by Hall-Jackson. Additionally, since everyone is susceptible to neurodegenerative disease, it would have been obvious to administer c-Raf inhibitors to inhibit neuronal cell death. Therefore, the rejection under 35 U.S.C 103(a) is deemed proper. Applicants argue that epilepsy is not a neurodegenerative disease. This argument has been fully considered and is persuasive. However, as taught by Roux (p75 Neurotrophin Receptor Expression is induced in Apoptotic Neurons after Seizure, Journal of Neuroscience, August 15, 199, 19(16); pages 6887-6896) of record expressly teaches in the abstract that seizures causes neuronal cell loss in both animal model and human epilepsy. And that determination of the contribution of apoptotic mechanism to seizure-induced neuronal cell death. Therefore, seizures do in fact cause neuronal cell loss as demonstrated by Roux. And since everyone is susceptible to neurodegenerative disease, it would have been obvious to administer c-Raf inhibitors to inhibit neuronal cell death to

/San-ming Hui/  
Primary Examiner, Art Unit 1628

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